| Office Action Summary | Application No. | Applicant(s) |
|---|---|---|
| | 09/622,452 | WEINER ET AL. |
| | Examiner | Art Unit |
| | ANNE MARIE S. WEHBE | 1633 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *3/15/11*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,4,6,7,9-12,15,17,18,33,36,42,43,46,49,50 and 52-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-7,12,17,33,46,49,53-54,and 56* is/are rejected.

7)☒ Claim(s) *1,4,6,7,9-12,15,17,18,33,36,42,43,46,49,50 and 52-58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

| Attachment(s) | |
|---|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ . |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) ☐ Notice of Informal Patent Application |
| 3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____. | 6) ☐ Other: _____. |

## DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, including an amendment and response, filed on 3/15/11 has been entered. Claims 2-3, 5, 8, 13-14, 16, 19-32, 34-35, 37-41, 44-45, 47-48, and 51 are canceled. Claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-43, 46, 49-50, and 52-58 are currently pending and under examination in the instant application based on the elected species of "DR5" as the immunomodulating protein. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

### *Claim Rejections - 35 USC 102*

The rejection of claims 1, 6, 12, 17, and 53-54 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, is withdrawn over claims 1, 6, and 53 in view of applicant's amendment to claim 1 which limits the immunogen to an HIV or herpes simplex antigen, and maintained over claims 12, 17, and 54. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below.

The applicant reiterates their previous argument that Alnemri et al. does not teach a "pyrogen free" composition, and that the skilled artisan reading Alnemri et al. would not expect that the sterile compositions taught by Alnemri et al. would be pyrogen free. The applicant has further supplied the US FDA's guidelines for endotoxin testing and states that such extraordinary procedures are not undertaken for materials used in rodent studies.

In response, Alnemri et al. clearly teaches a plasmid encoding DR5 and the immunogen LacZ, which is a bacterial antigen, i.e. an immunogen which is a pathogen antigen, or the combination of the plasmid encoding DR5 and the plasmid encoding CrmA, a viral protein antigen which is also an immunogen derived from a pathogen, and further provides teachings for making a sterile aqueous solution in columns 22-23. Note that as there is no requirement that the a prior art reference must set forth the claimed invention *in haec verba,* it is irrelevant that Alnemri et al. does not use the phrase "pyrogen free" as Alnemri et al. clearly teaches sterile aqueous solutions of the disclosed plasmids which meet the definition of "pyrogen free", as discussed in detail in previous office actions. In particular, the previous office action discussed that fact that Alnemri broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid and water or physiological saline (column 23, lines 12-17). Since Alnemri et al. teaches that the solution does not contain anything other than nucleic acid and water or physiological saline, the solution cannot by Alnemri's own definition contain a pyrogen. Thus, the solutions taught by Alnemri et al. qualify as "pyrogen-free".

In regards to the FDA's standards for human clinical applications, it is noted that there is no limitation in the claims regarding human administration of the preparation of the composition

to meet FDA guidelines and standards. The claims as written recite a "pyrogen-free" composition, and as such it is maintained that Alnemri et al. teaches such a composition.

Therefore, for reasons of record as discussed in detail above, the rejection stands.

***Claim Rejections - 35 USC § 103***

The rejection of claims 1, 6, 12, 17 and 53-54 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, in view of U.S. Patent No. 5,693,622 (12/2/97), hereafter referred to as Wolff et al. is withdrawn over claims 1, 6, and 53 in view of applicant's amendment to claim 1 which limits the immunogen to an HIV or herpes simplex antigen, and maintained over claims 12, 17, and 54. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below.

The applicant reiterates their previous arguments that there is no motivation to make a pyrogen free plasmid encoding DR5 in either Alnemri or Wolff. In response, Alnemri specification broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid, water or physiological saline. Thus the teachings in column 22 to prepare sterile aqueous solutions of the nucleic acids reads on the particular plasmids disclosed in the examples, which include a single plasmid encoding DR5 and the bacterial pathogen immunogen LacZ or the combination of a plasmid encoding DR5 and a plasmid encoding CrmA, a viral pathogen antigen, regardless of whether they were actually used in *in vitro* experiments versus *in vivo* methods. Wolff et al. was

further cited to provide teachings for the standard methods of preparing plasmid DNA for pharmaceutical use. Therefore, it is maintained that in view of the teachings of Alnemri et al. to prepare a sterile composition comprising a plasmid(s) encoding DR5 for administration to a mammal, and the teachings of Wolff et al. for standard methods for plasmid DNA preparation for *in vivo* use, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use the well known and widely practiced methods taught by Wolff et al. to prepare the plasmids encoding DR5 and an immunogen taught by Alnemri et al.. Further, based on the standard nature of cesium chloride purification, and the high level of skill in the art of molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in producing a pyrogen-free composition containing the plasmid(s) taught by Alnemri et al. using the purification method taught by Wolff et al. Therefore, the rejection of record is maintained.

Applicant's amendments to the claims has necessitated the following new grounds of rejection under 35 U.S.C. 112, second paragraph, and fourth paragraph.

***Claim Rejections - 35 USC 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. Claim 53 depends on claim 1 which has been amended to limit the pathogen antigen is an HIV or herpes simplex antigen. As such, claim 53, which recites that the antigen is a viral antigen conflicts with the limitations of claim 1 as "a viral antigen" is broader genus of antigens than HIV or herpes simplex antigens. Thus, the limitation of claim 53 conflicts with the limitations of claim 1 as it recites a broader genus of antigens than encompassed by claim 1. Therefore, the metes and bounds of the claim cannot be determined.

The following is a quotation of the fourth paragraph of 35 U.S.C. 112:

> Subject to the [fifth paragraph of 35 U.S.C. 112], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Claim 53 is rejected under 35 U.S.C. 112, 4th paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends, or for failing to include all the limitations of the claim upon which it depends. Claim 53 depends on claim 1 which has been amended to limit the pathogen antigen is an HIV or herpes simplex antigen. As such, claim 53, which recites that the antigen is a viral antigen, does not further limit claim 1. Applicant may cancel the claim(s), amend the claim(s) to place the claim(s) in proper dependent form, rewrite the claim(s) in independent form, or present a sufficient showing that the dependent claim(s) complies with the statutory requirements.

***Duplicate Claims***

Applicant is advised that should amended claim 7 be found allowable, claim 33 and claim 56 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof; should claim 55 be found allowable, claim 57 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof ; and should claim 52 be found allowable, claim 58 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof . When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

***Claim Objections***

Claims 15, 18, and 42-43 are objected to as being dependent upon a rejected base claim, but would be allowable based on the elected species of DR5 as the immunomodulating protein if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

**Further, as set forth in previous actions in the interests of compact prosecution, it is again noted that should applicant limit claims 1, 4, 6-7, 9-11, 15, 18, 33, 36, 42-43, 46, 49-50, 52, and 55-58 to the elected subject matter of DR5, and rewrite all claims dependent on rejected claims 12, 17, or 54 in independent form as noted in the preceding paragraph, the subject matter of claims 1, 4, 6-7, 9-11, 15, 18, 33, 36, 42-43, 46, 49-50, 52, and 55-58 would be considered free of the prior art of record and allowable.**

The objection to pending claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-43, 46, 49-50, and 52-58 for continuing to recite non-elected subject matter, there being no allowable generic claim, is maintained. The applicant argues that all the claims recite the elected species and that once this species is found to be allowable that the generic claims and a reasonable number of non-elected species be examined and allowed. In response, it is first noted that all the instant claims have not been found allowable based on examination of the elected species of DR5. Further, MPEP 809.02(a) states:

> Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

As the generic claims have not been found allowable, see below, the objection to the claims remains.

In the interests of compact prosecution and in an attempt to further prosecution the examiner has made several rejections of record over the generic claims in previous office actions to demonstrate that the generic claims are not allowable. However, the previous office actions clearly stated that the election of species requirement has NOT been withdrawn, and full examination of the claims remains based on the elected species of DR5 as the immunomodulatory molecule. It is further noted that applicant's amendment of the claims to delete ICAM-1 as the immunomodulating protein does not render the generic claims allowable, see below.

The rejection of claims 1, 6, 33, 46, 49, and 56 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,916,879 (1999), hereafter referred to as Webster, in view of US Patent No. 5,990,301 (1999), hereafter referred to as Colpan et al., is withdrawn over amended claims 1 and 6 which now limit the pathogen antigen to an HIV or herpes simplex antigen, and maintained over amended claims 33, 46, 49, and 56. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the claims have been amended to delete ICAM-1 as the immunomodulatory molecule and that Webster et al. doesn't teach any of the other recited species. However, please note that Webster et al. does indeed teach other immunoeffectors, including IL-7. Specifically, Webster teaches one or two plasmids encoding influenza HA and an immunoeffector, and further wherein the immunoeffector is IL-7 (Webster, columns 6, 11-12, and 18). Webster further teaches the plasmid or plasmids wherein one or both genes are operatively linked to a CMV promoter (Webster, columns 4, 11-12). In addition, Webster teaches methods of generating protective immunity against influenza virus in a subject by intramuscular administration of the plasmid(s) encoding HA and an immunoeffector such as IL-7 (Webster, columns 4-6, and 16-18).

Therefore, applicant's amendments to the claims does not overcome the rejection of record.

In view of applicant's amendments to claims 1 and 6, the following rejection is made of record.

Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prayaga et al. (1997) Vaccine, Vol. 15 (12/13), 1349-1352, in view of U.S. Patent No. 5,916,879 (1999), hereafter referred to as Webster, and US Patent No. 5,990,301 (1999), hereafter referred to as Colpan et al.

Prayaga et al. teaches a composition comprising two plasmids, where the first plasmid encodes the HIV antigen gp120 under expression control of the CMV promoter and the second plasmid encodes the co-stimulatory molecule IL-7 under expression control of the CMV promoter (Prayaga et al., page 1350). Prayaga et al. further teaches the administration of a pharmaceutical composition of the plasmids to induce Th1 T cell responses and antibody responses against gp120 (Prayaga et al., pages 1350-1351).

Prayaga et al. differs from the instant composition by not teaching to include the sequences encoding the gp120 antigen and IL-7 in a single plasmid and further to prepare a pyrogen free composition comprising the plasmid. However, at the time of filing, Webster teaches one or two plasmids encoding a viral antigen and an immunoeffector such as IL-7 can be used to generate protective immunity against a virus in a subject (Webster, columns 4-6, 11-12 and 16-18). Webster further teaches the plasmid or plasmids wherein one or both genes are operatively linked to a CMV promoter (Webster, columns 4, and 11-12). Webster also teaches to purify the plasmid DNA for administration using Qiagen columns (Webster, columns 20-21). However, Webster does not specifically teach the level of purity of the plasmid DNA obtained. Colpan et al. supplements Prayaga et al. and Webster et al. by teaching particular Qiagen columns and methods which provide toxin-free, including endotoxin free, preparations of

plasmid DNA suitable for therapeutic administration of genetic vaccines (Colpan et al., columns 3-5, and 9-10). Colpan et al. further teaches that their disclosed and claimed methodology is preferable to other methods of purification since the plasmid DNA obtained is free of allergic, toxic, and possibly carcinogenic substances including phenol, chloroform, ethidium bromide, and endotoxins (Colpan et al., columns 3-4).

Thus, in view of the teachings of Webster that either a single plasmid or two separate plasmids can be used to encode a viral immunogen and IL-7 for use in genetic immunization, the further teachings of Webster et al. to purify plasmid DNA using a Qiagen column, and the detailed teachings of Colpan et al. for an improved method of Qiagen plasmid DNA preparation which produces endotoxin free plasmid preps for genetic vaccination, it would have been *prima facie* obvious to the skilled artisan to prepare a single plasmid as taught by Webster which encodes gp120 and IL-7 as taught by Prayaga et al. using the method disclosed by Colpan et al. in order to produce a purified plasmid preparation suitable for vaccination of a subject with a reasonable expectation of success.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center

fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

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